

~~Sub B1~~

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1 A method for determining whether a test compound modulates the
2 drug resistance of a cell, the method comprising:
3 a) determining the level of MDA-9 expression in a cell in the presence of a
4 test compound;
5 b) determining the level of MDA-9 expression in the cell in the absence of the
6 test compound; and
7 c) identifying the compound as a modulator of drug resistance of the cell if the
8 level of expression of MDA-9 in the cell in the presence of the test compound differs
9 from the level of expression of MDA-9 in the cell in the absence of the test compound.

1 2. The method of claim 1 wherein the MDA-9 is encoded by an
2 endogenous gene.

1 3. A method for determining whether a test compound modulates the
2 drug resistance of a cell, the method comprising:
3 a) incubating MDA-9 protein in the presence of a test compound;
4 b) determining whether the test compound binds to the MDA-9 protein;
5 c) selecting a test compound which binds to the MDA-9 protein;
6 d) administering the test compound selected in step c) to a non-human
7 mammal having drug resistant cells;
8 e) determining whether the test compound alters the drug resistance of the
9 cells in the non-human mammal; and
10 f) identifying the test compound as a modulator of drug resistance of the cell if
11 the compound alters the drug resistance of the cells in step (e).

in vivo

1 4. A method for determining whether a test cell has a drug-resistant
2 phenotype, the method comprising:
3 a) measuring the expression of MDA-9 in the test cell;
4 b) comparing the expression of MDA-9 measured in step a) to the expression
5 of MDA-9 in a control cell not having a drug-resistant phenotype; and

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6 c) determining that the test cell has a drug resistant phenotype if the
7 expression of MDA-9 in the test cell is greater than the expression of MDA-9 in the
8 control cell.

1 ~~5.~~ A method of determining whether a test cell has a drug-resistant
2 phenotype, the method comprising:
3 a) measuring the activity of MDA-9 in the test cell;
4 b) comparing the activity of MDA-9 measured in step a) to the activity of
5 MDA-9 in a control cell not having a drug-resistant phenotype; and
6 c) determining that the test cell has a drug resistant phenotype if the activity of
7 MDA-9 in the test cell is greater than the activity of MDA-9 in the control cell.

1 ~~6.~~ A method for determining whether a subject has or is at risk of
2 developing a drug resistant tumor, the method comprising:
3 a) measuring the expression of MDA-9 mRNA in a biological sample
4 obtained from the subject;
5 b) comparing the expression of MDA-9 mRNA measured in step a) to the
6 expression of MDA-9 mRNA in a biological sample obtained from a control subject not
7 having a drug resistant tumor; and
8 c) determining that the patient has or is at risk of developing a drug resistant
9 tumor if the expression of MDA-9 mRNA in the biological sample obtained from the
10 patient is higher than the expression of MDA-9 mRNA in the biological sample obtained
11 from the control subject.

1 7. The method of claim 6, wherein step a) comprises the use of a nucleic
2 acid molecule that hybridizes to MDA-9 mRNA.

1 ~~8.~~ A method for determining whether a subject has or is at risk of
2 developing a drug resistant tumor, the method comprising:
3 a) measuring the activity of MDA-9 in a biological sample obtained from the
4 subject;

5 b) comparing the activity of MDA-9 measured in step a) to the expression of
6 MDA-9 mRNA in a biological sample obtained from a control subject not having a drug
7 resistant tumor; and

8 c) determining that the patient has or is at risk of developing a drug resistant
9 tumor if the activity of MDA-9 in the biological sample obtained from the patient is
10 higher than the activity of MDA-9 in the biological sample obtained from the control
11 subject.

1 9. The method of claim 8, wherein step a) comprises the use of an agent
2 that binds to MDA-9 protein.

1 10. A method for monitoring the effect of an anti-tumor treatment on a
2 patient, the method comprising:

3 a) measuring the expression of MDA-9 in a tumor sample obtained from the
4 patient;

5 b) comparing the expression of MDA-9 measured in step a) to the expression
6 of MDA-9 in a control sample of cells; and

7 c) determining that the anti-tumor treatment should be discontinued or
8 modified if the expression of MDA-9 in the tumor sample is higher than the expression of
9 MDA-9 in the control sample of cells.

1 11. The method of claim 10, wherein step a) comprises the use of a nucleic
2 acid molecule that hybridizes to MDA-9 mRNA.

1 12. A method for monitoring the effect of an anti-tumor treatment on a
2 patient, the method comprising:

3 a) measuring the activity of MDA-9 in a tumor sample obtained from the
4 patient;

5 b) comparing the activity of MDA-9 measured in step a) to the activity of
6 MDA-9 in a control sample of cells; and

7 c) determining that the anti-tumor treatment should be discontinued or
8 modified if the activity of MDA-9 in the tumor sample is higher than the activity of
9 MDA-9 in the control sample of cells.

1 13. The method of claim 12, wherein step a) comprises the use of an agent
2 that binds to MDA-9 protein.

1 14. A method for modulating the drug resistance of a cell, the method
2 comprising modulating MDA-9 expression within the cell.

1 15. A method reducing the drug resistance of cell, the method comprising
2 contacting the cell with a molecule which reduces the expression of MDA-9 within the
3 cell.

1 16. A method of increasing the effectiveness of a chemotherapeutic
2 compound in a patient suffering from a disorder associated with the presence of drug-
3 resistant neoplastic cells, the method comprising:
4 a) administering a chemotherapeutic compound to the patient; and
5 b) administering a compound with reduces MDA-9 expression to the patient.

1 17. A method of treating a mammal suspected of having a disorder associated
2 with the presence of drug-resistant cells, the method comprising administering to the
3 mammal a compound that reduces the expression of MDA-9 in the drug-resistant cells,
4 the reduction be sufficient to reduce the drug resistance of the drug resistant cells.

1 18. A method for increasing the drug resistance of cell that has an undesirably
2 low level of MDA-9 expression, the method comprising exposing the cell to a compound
3 that increases the expression of MDA-9.

1 19. A method for treating a drug resistant tumor in a patient, the method
2 comprising administering to said subject an amount of a MDA-9 antagonist effective to
3 reduce drug resistance of said tumor in the patient.

